Cofabrication: A Strategy for Building Multicomponent Microsystems

Co-Fabrication: A Strategy for Building Multi-Component Microsystems

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Conspectus

This account describes a strategy for fabricating multi-component microsystems that forms the structures of all (or essentially all) of the components of these systems in a *single* step of micromolding (Figure 1). This strategy—which we call "co-fabrication"—is an alternative to multi-layer microfabrication, in which multiple layers of components are sequentially aligned ("registered") and deposited on a substrate, using photolithography to form the patterns in these layers.[1]

Co-fabrication has several characteristics that make it a particularly useful approach for building multi-component microsystems. It generates correctly aligned components (e.g., wires, heaters, magnetic field generators, optical waveguides, microfluidic channels, etc.) rapidly, inexpensively and over very large surface areas. By avoiding the use of registration, the technique does not require that devices adhere to the restrictions on the size of substrates imposed by common registration tools such as steppers and contact aligners. We have demonstrated multi-component microsystems with surface areas >100 cm^2, but in principle there should be no limitation in surface area other than that of generating the original master.

Co-fabrication can also serve as a low-cost and/or minimal equipment strategy for building microsystems. The technique is accessible to users in a variety of laboratory settings and can be performed using fabrication tools that are less expensive than those used for multi-step microfabrication. The process also requires only small amounts of solvent and photoresist—a costly chemical required for photolithography. In co-fabrication, photoresist is applied and developed only once to produce a master, which is then used to produce multiple copies of molds containing the microfluidic channels.

At a more general level, co-fabrication represents a new processing paradigm in which the exterior (or shell) of the desired structures are produced before the interior (or core). This approach—generating the insulation or packaging structure first, and injecting materials that provide function in channels in *liquid phase*—makes it possible to design and build microsystems using component materials that cannot be used easily in conventional procedures (e.g., solid materials with low melting points, liquid metals, liquid crystals, fused salts, foams, emulsions, gases, polymers, biomaterials, fragile organics), or whose materials can be altered, removed, or replaced *after* the manufacturing stage. For example, co-fabrication allows one to build devices in which a material—such as a liquid—flows through the device during use, or is replaced before use, or in which a material—such as a metal wire—can be melted and re-set by heating (and thus, in principle, repair a break in the device). This method leads to certain kinds of structures—such as integrated metallic wires with large cross-sectional areas, or optical waveguides aligned in the same plane as microfluidic channels—that would be difficult or impossible to make using techniques such as sputter deposition or evaporation.

This account outlines the strategy of co-fabrication, and describes several microsystems fabricated using this approach that combine microfluidics with: (i) electrical wires for microheaters, electromagnets, and organic electrodes; (ii) fluidic optical components, such as optical waveguides, lenses, and light sources; (iii) gels for biological cell cultures, and (iv) droplets for compartmentalized chemical reactions, such as protein crystallization.

I. Fabricating Microfluidic Channels

Co-fabrication starts with the design and fabrication of a single layer (or plane) of microfluidic channels. Microchannels in PDMS can be readily produced using soft lithography.[2,3] Using this approach, a master is first created by patterning photoresist using contact photolithography. To reduce costs for features having relatively large (>10 μm) dimensions, a transparency with the desired patterned printed with a high resolution printer can be used as the photomask. Subsequent casting of the PDMS pre-polymer against the master and curing yields the polymer replica with a network of channels. Bringing the polymer replica in conformal contact with a flat slab of PDMS (or other substrates including glass, oxidized silicon, or oxidized polystyrene) after oxidization of both surfaces irreversibly seals and completes the microchannels. The procedure for fabricating the channels takes less than 24 h from computer design to physical system.

For some applications, it is desirable to build the layer of microfluidic channels using a material other than PDMS.[4,5] For example, bulk and surface micromachining[6] rely on dry- or wet-etching cavities in silicon or glass substrates, followed by a bonding step with another surface. Microinjection molding, micro-imprinting/embossing, and laser ablation are commonly used to produce microfluidic channels in plastics and other polymers.[7-9] Scanning beam lithography techniques, such as focused ion-beam, e-beam, and pulsed laser deposition can fabricate microchannels as small as 10 nm in width.[10,11] Patterning paper into hydrophobic and hydrophilic regions also provides a new approach to the fabrication of microfluidic channels.[12]

Ultimately, the choice of material used for microfluidic channels (e.g., the *bas-relief material* of a co-fabricated system) depends on the characteristics required of that

material in the final application: temperature stability, elasticity, transparency, resistance to solvent, permeability, wettability, biocompatibility, scalability, index of refraction, etc. Table 1 summarizes materials often used for generating microfluidic channels.

II. Filling Microfluidic Channels with Materials

Microfluidic channels are typically filled with liquids using either capillary action, or active injection by pump/vacuum. Capillarity depends on the relative free energies of the interfaces in a channel to "wick" aqueous fluids in microfluidic channels.[13] It is also possible to fill channels by applying an external vacuum or pressure to force a material in the channel; this approach is especially useful for replacing fluids in previously-filled channels, or for applications in which the fluid must flow through the channel to provide function (e.g., optofluidics).

Microfluidic channels can be filled with solid materials by injecting the material in the channel in liquid form, and then allowing the material to solidify inside the channel. We have found it particularly useful to be able to inject molten metals and alloys (e.g., In, Sn, Ga, In/Sn, In/Ag, Ga/In) into microfluidic channels by heating the metals and channels using a hotplate and/or heat gun, drawing the metal in the channel using house vacuum, and allowing the metal to solidify by cooling; PDMS is able to withstand temperatures up to 400 ºC for limited times.[14] It is also possible to inject liquid materials into microfluidic channels, and to solidify these liquids into solids by curing or chemical cross-linking. These materials include sol-gels,[15,16] thermally curable

epoxies,[17,18] and photocurable pre-polymers.[19] Crystallization in microfluidic channels has also been demonstrated.[20] (Table 2).

For some materials, it is necessary to modify the interior surface of the microfluidic channels chemically to improve the wettability of the injected material. For example, prior to injecting low-melting point metal (e.g., In) or metal alloy (e.g., eutectic In/Sn) into a PDMS channel to form a long, continuous wire, it is first necessary to oxidize the surface of the channel, and then to modify it with a silane (3-mercaptopropyltrimethoxysilane) so that the metal wets it.[14] When injected into untreated PDMS channels, most metals in liquid form do not wet the walls of the channels. As a result, they tend to fracture upon cooling and solidification, and to lose their electrical connectivity/conductivity.

III. Devices Produced Using Co-Fabrication

This section describes several devices that demonstrate the design, operation, and characterization of co-fabricated microsystems.

Liquid-filled Channels (Microfluidics)

Over the past decade, the study of the flow of liquids in microfluidic channels and the applications of liquid-filled microchannels has emerged as an area of great scientific and technological interest.[21,22] A number of groups have investigated and modeled the physics of microfluidic laminar flow in microsystems.[23,24] Microfluidic channels filled with media are useful for the study of cells[25,26] or whole microorganisms.[27] Liquid-

filled channels have been applied for the development of a variety of practical "lab-on-a-chip" devices including devices for high-throughput analysis,[28,29] generation of chemical gradients,[30] fluidic mixing,[31], and detection and diagnosis of disease.[32,33]

Metal-filled Channels (Microsolidics)

A growing interest in automated lab-on-a-chip systems has fueled the development of microfluidic systems in which metal wires provide electronic function to the system.[34] Using the principles of co-fabrication, we have produced current-carrying wires by injecting liquid metal in microfluidic channels and allowing the metal to cool and solidify;[14] for very low melting temperature metals, we also used the metal directly in liquid form.[35] This method of fabrication—which we call *microsolidics*—ultimately generates *solid* metal structures in two or three dimensions that can be fabricated in close alignment with microfluidic channels (Figure 2). The wires can be fabricated with high aspect ratios and cross sectional areas up to 10×10^6 μm^2; this large cross-sectional area is difficult to achieve in a small footprint using alternative techniques such as evaporation or sputter deposition, and makes it possible to use the wires for applications requiring high electrical current (e.g., for generation of magnetic fields). The general procedure consists of five steps: (i) fabrication of microfluidic channels in PDMS using soft lithography and rapid prototyping; (ii) plasma oxidation and silanization of the inside surfaces of the microchannels with 3-mercaptopropyltrimethoxysilane (0.1 M solution in acetonitrile) to make them wettable to the metals we use; (iii) introduction of molten metal into the channels by applying a vacuum to draw metal into the channels—walls of silanized channels are rapidly wet, for example, by liquid indium, eutectic indium-tin, or

eutectic gallium-indium, walls of unmodified channels are not; (iv) cooling the channels to form solid metal microstructures; and (v) (if desired) forming the solder-filled system of channels into non-planar topologies by bending, twisting, rolling, or deforming. This last step—modifying the shape—works particularly well when the metal is encapsulated in thin (50-200 μm) layers of PDMS. Using this technique, it is possible to fabricate metallic structures with lateral dimensions as small as 50 μm, and thicknesses of 10 μm – 1 mm. Because the structures are embedded in polymer insulation, breaks or fractures in the metal can often be repaired by heating the metal above its melting point and cooling (perhaps with brief sonication).

Microheaters. Microsolidic wires can be used to build precision-integrated heaters for microfluidic channels.[14] Indium metal (100%) was injected in microfluidic channels and cooled to form solid, resistive metal wires in microchannels 100 μm × 100 μm in cross-sectional area. Passing electrical current through the wires increased the temperature of the metal by Joule heating, which, in turn, increased the temperature of adjacent microfluidic channels. Microsolidic heaters with cross-sectional areas of 10^4 μm^2 supported currents up to 2 A (2×10^8 $A \cdot m^{-2}$) without breaking down, and have been shown to heat static or flowing aqueous fluids in adjacent microfluidic channels to >100 ºC.

In-plane electromagnets. Microsolidic wires have also been used to build integrated electromagnets for separations (Figure 3).[36,37] Siegel et al. co-fabricated metal wires in close proximity (distance ~10 μm) to liquid-filled microfluidic channels. Passing electrical current through the wires generated magnetic fields up to 2.8 mT and magnetic field gradients up to 40 $T \cdot m^{-1}$, orthogonal to the direction of current flow.

These gradients captured/released and sorted superparamagnetic beads suspended in the adjacent liquid-filled microfluidic channels with forces up to 3.3 pN.

Liquid-Liquid Optical Systems

The principles of co-fabrication can also be applied to fabricate reconfigurable optical components.[38,39] One category of these devices, which we call liquid-liquid (L^2) systems, typically comprise two or more streams of liquid flowing in microfluidic channels, each possessing different optical properties (such as refractive indices) (Figure 4a). At low and moderate Reynolds numbers, flow of these streams is laminar;[22] this property creates optically smooth L^2 interfaces which exhibit low optical losses from scattering.

Liquids can be replaced and/or replenished continuously in L^2 systems. This capability for replacement allows injection of liquids with different properties (e.g., index of refraction, absorption, fluorescence) to tune the optical output of a microsystem in real time. The ability to replenish liquids minimizes the impact of photobleaching and related phenomena, because bleached elements are replaced continuously. In addition, the L^2 interface is deformable: by manipulating the flow conditions—for example, the relative volumetric rates of flow between the streams of liquids—it is possible to change the position or the shape of the liquid-liquid interface, and therefore, the path of light inside the optofluidic devices.

Optofluidic waveguides. Optical waveguides can be formed in microfluidic channels in which the laminar streams, themselves, control the direction of the flow of light.[38] These devices consist of two streams of liquids with lower refractive index (the

cladding) sandwiching a stream of liquid with higher refractive index (the core) in a single microchannel; light is supplied from an optical fiber inserted in PDMS through a fiber port fabricated at the end of the channel (Figure 4b). By controlling the relative rates of flow of the core and cladding liquids, we changed the width of the core stream, and therefore, the width of the optical waveguide. Decreasing the ratio of flow rates of the core to the cladding streams decreased the core size from >100 μm to <10 μm, and switched the guiding from multi- to single-mode.

Optofluidic switches and couplers. Co-fabricated liquid-liquid components can be used to build complex devices that control the direction of propagation of light in microfluidic channels.[38] We built an optical switch by branching an L^2 waveguide into three separate outlet channels (Figure 4c). Changing the relative rates of flow of the cladding liquids changed the path of the core liquid, and therefore, the path of the light. It was also possible to fabricate an evanescent coupler comprising two L^2 waveguides sharing an inner cladding stream with a width < 5 μm. Light from an optical fiber was introduced into one of the L^2 waveguides. The efficiency of coupling of evanescent fields between the two waveguides was modified by changing the rate of flow of the liquids, which in turn, adjusted the width of the inner cladding stream. Efficient coupling was observed when the width of the inner cladding was <2 μm.

Optofluidic lenses. Fabrication of tunable on-chip microlenses is a challenge in optics research. We used the principles of co-fabrication to build a liquid-liquid lens, where the curvature of the interface could be modified dynamically (Figure 5a).[40] The lens was formed by laminar flow of three streams of fluids in a microchannel; the index of refraction of the core stream was higher than the index of the cladding streams. The

streams entered an “expansion chamber”, or a region of the microchannel with increased width. For appropriate rates of flow, the shape of the interface between the core and cladding streams in this region was biconvex; this structure focused light propagating in the plane of the expansion chamber perpendicular to the direction of flow of the liquids. Changing the relative rates of flow of the three streams modified the curvature of the interface—and thus the focal distance of the lens—in real time.

Optofluidic light sources. We developed various on-chip fluidic light sources based on the liquid-liquid waveguide systems for optical detection and spectroscopic analysis in integrated microanalytical systems (μTAS).[41,42] In these systems, solutions containing fluorescent dye flowed through microchannels and were excited optically by incident light from an external halogen bulb or a pump laser (Figures 5b,c). Microchannel-based fluorescent light sources circumvent the need to align and secure optical fibers to microfluidic channels, and can be produced with a range of cross-sectional diameters.

Electronic Interfacing with Surfaces

Sometimes it is possible to gain additional function in a co-fabricated system by placing the layer of microfluidic channels—roughly and with minimal precision—perpendicular to a chemically patterned surface. We co-fabricated an array of seven molecular-scale tunnel junctions[43] each comprising an electrically conductive self-assembled monolayer (SAM) connected to two metallic electrodes via a microfluidic channel (Figure 6a).[44] We aligned a PDMS microchannel perpendicularly to Ag electrodes on a glass substrate and sealed it to the surface; the Ag electrodes were patterned with $SC_{11}Fc$ (Fc = ferrocene) SAMs. Injecting liquid metal (EGaIn = eutectic

Ga-In)[45] in the microchannel formed electrical contact between the SAM-Ag electrode pair and completed the molecular junction. An optical micrograph of the devices is shown in Figure 6b. The resulting Ag-SC_{11}Fc//EGaIn junctions ('-' indicates a covalent bond and '//' indicates a van der Waals contact) rectified currents with rectification ratios R ($R = |J(-V)|/|J(+V)|$, J = current density (A/cm^2), V = the voltage (V)) of 102 at $V = \pm$ 1.0 V. The electrodes and microfluidic channel were arranged in a 7 × 1 cross-bar scheme (comprising seven Ag electrodes and one EGaIn-filled microfluidic channel).

The co-fabricated tunnel junctions gave working devices in ~80% yield, and reliably rectified AC electronic signals.[44] Figure 6c shows the average current density as a function of the potential of the tunnel junctions. These results represent a first step in applying co-fabrication to produce functional molecular electronic devices in microfluidic channels.

In-channel Gels for Electrophoresis and Cellular Growth

Co-fabrication of gels and other multi-phase materials in a single layer of microfluidic channels produces microdevices with useful function in biology. Typically, gels are injected in the channels in liquid form, and then cured by heating, cooling, or UV irradiation. A variety of groups have injected polyacrylamide gels in microfluidic channels or networks of channels for applications in 1D and 2D electrophoretic separation.[46,47] Other types of gels, including collagen- and acrylate-based hydrogels have been injected in microfluidic channels for microfluidic valving and flow control,[48] colorimetric molecular sensing,[49] tissue engineering,[50,51] and for constructing cellular and biomolecular microenvironments.[52-55]

Bubble and Droplet Generation in Microchannels

There has been growing interest in producing emulsions such as foams in microfluidic devices.[56,57] We and others have used co-fabrication to generate monodisperse emulsions of bubbles,[58] droplets,[59] and polymer particles[60] in microchannels that exhibit remarkable regularity. Flow-focusing[58,60] and T-junction[59] geometries allow the user to tune the size and the fraction of volume that the bubbles and droplets occupy in the outlet channel. Garstecki et al. demonstrated the self-organization of bubbles in a variety of ordered gas-liquid and liquid-liquid lattices in microfluidic channels.[58] The form and structure of these lattices was adjusted by changing the pressures applied to the two immiscible fluids. These microfluidic lattices have four practical benefits. They are: i) self-organizing, (ii) self-healing, (iii) dynamically addressable, and (iv) made from components that are constantly replenished for real-time control and modification of the lattice.

Complex, periodic emulsions. Co-fabricating multiple flow-focusing generators in single layer of microfluidic channels makes it possible to produce complex, periodic structures of bubbles and droplets (Figure 7a).[61] The generators—when placed in close proximity to each other—allow fluctuations in the local fluidic resistance in a single channel, or in a network of channels, and thus make possible the synchronization of timing in formation of droplets and bubbles. This synchronization can produce stable, composite structures comprising different emulsions (droplets or bubbles) in the same continuous phase.[58] In one application of this approach, Hashimoto et al. used the self-organization of bubbles to produce microfluidic diffraction gratings.[62] Changing the external flow parameters (i.e., the rate of flow of water, and the applied pressure of

nitrogen) adjusted the diameter of the bubbles that were generated from the flow-focusing geometry (and thus, the lattice constant of the grating structure), and made it possible to tune the angle of diffraction of light from the device *dynamically* and in real time.

Chemical reactions in droplets. Droplets formed by flowing immiscible fluids in co-fabricated microfluidic channels can be used as vehicles for performing chemical reactions (Figure 7b).[63,64] Compartmentalization in droplets allows for the rapid mixing of reagents, provides precise control of the timing of reactions, and makes it possible to synthesize and transport solid products. Ismagilov and co-workers applied this strategy to the crystallization of proteins in microfluidic channels (Figures 7c).[65] The crystallization trials were set up inside 7.5-nL aqueous droplets, each containing solutions of protein, precipitants, and additives in variable ratios. This method allowed researchers to set up hundreds of crystallization trials under computer control at rates of several trials per second.

IV. Expanding Capabilities Through Co-Fabrication: Other Materials

Co-fabrication is already a useful technique for a variety of applications in science and technology. We believe, however, that many new applications will emerge when new materials (and combinations of materials) are injected as gases or liquids into microchannels. Table 2 suggests several possibilities, some of which have been demonstrated, and some of which have not. In co-fabrication, structural and functional elements are added to channels after the channels are formed, and, hence, the only factor limiting a choice of materials is the ability to fill a channel with them. In the future, we

envision systems comprising high-melting-temperature materials such as glasses, structural metals, or temperature-resistant polymers (both for the channels themselves, and for the materials that fill the channels), and systems based on novel materials that are formed by combining two or more substances in a microfluidic channel (e.g., combination of PDMS and Fe_3O_4 to produce functional ferromagnetic ceramics). The integration and micron-scale registration of these new materials may lead to a variety of practical applications not-yet-seen in meso- and micro-scale engineering.

V. Conclusions

Co-fabrication represents a new model for designing and building multi-component microsystems. The approach is especially applicable to technologies that require the integration and registration of multiple different materials in one or more layers with micron-precision, but where simplicity and economy of fabrication are key characteristics of the design process. We anticipate that advances in co-fabrication will lead to new, practical applications in energy storage (e.g., batteries), lab-on-a-chip systems, flexible electronics, systems biology, thermal management, self-standing 3-D structures (in which the surrounding insulation is removed after fabrication), and compound multilayer microsystems produced by combining several co-fabricated layers in a single device.

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Biographies

Adam C. Siegel received his B.S. degree in Electrical Engineering in 2001 from the University of Michigan at Ann Arbor. He received his M.S. degree (2004), and his Ph.D. (2009) from Harvard University under the direction of George M. Whitesides in the Department of Chemistry. His doctoral work focused on the design and fabrication of microsystems using unconventional materials such as silicones, paper, and plastics.

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Michael Dickey received his B.S. degree in Chemical Engineering in 1999 from Georgia Institute of Technology. His Ph.D. (2006) work at the University of Texas at Austin under the direction of Grant Willson focused on new patterning techniques such as imprint lithography. He recently completed a post-doctoral fellowship at Harvard University under the guidance of George Whitesides and is currently an assistant professor at NC State University.

George M. Whitesides was born August 3, 1939 in Louisville, KY. He received an A.B. degree from Harvard University in 1960 and a Ph.D. from the California Institute of Technology (with J.D. Roberts) in 1964. He was a member of the faculty of the Massachusetts Institute of Technology from 1963 to 1982. He joined the Department of Chemistry of Harvard University in 1982, and was Department Chairman 1986-89, and Mallinckrodt Professor of Chemistry from 1982-2004. He is now the Woodford L. and Ann A. Flowers University Professor.

Figure 1. Co-fabrication involves three steps: (i) designing the microsystem in such a way that a single layer of separate sub-systems of microfluidic channels provides the structural basis for all of the components and functions required in the final device, (ii) fabricating these channels by micromolding, and (iii) generating function by filling the separate sub-systems of microfluidic channels with appropriate functional materials in fluid form. In this example, a simple step of micromolding ultimately generates two independent, aligned metal wires, a microfluidic channel, and an optical structure.

Figure 1

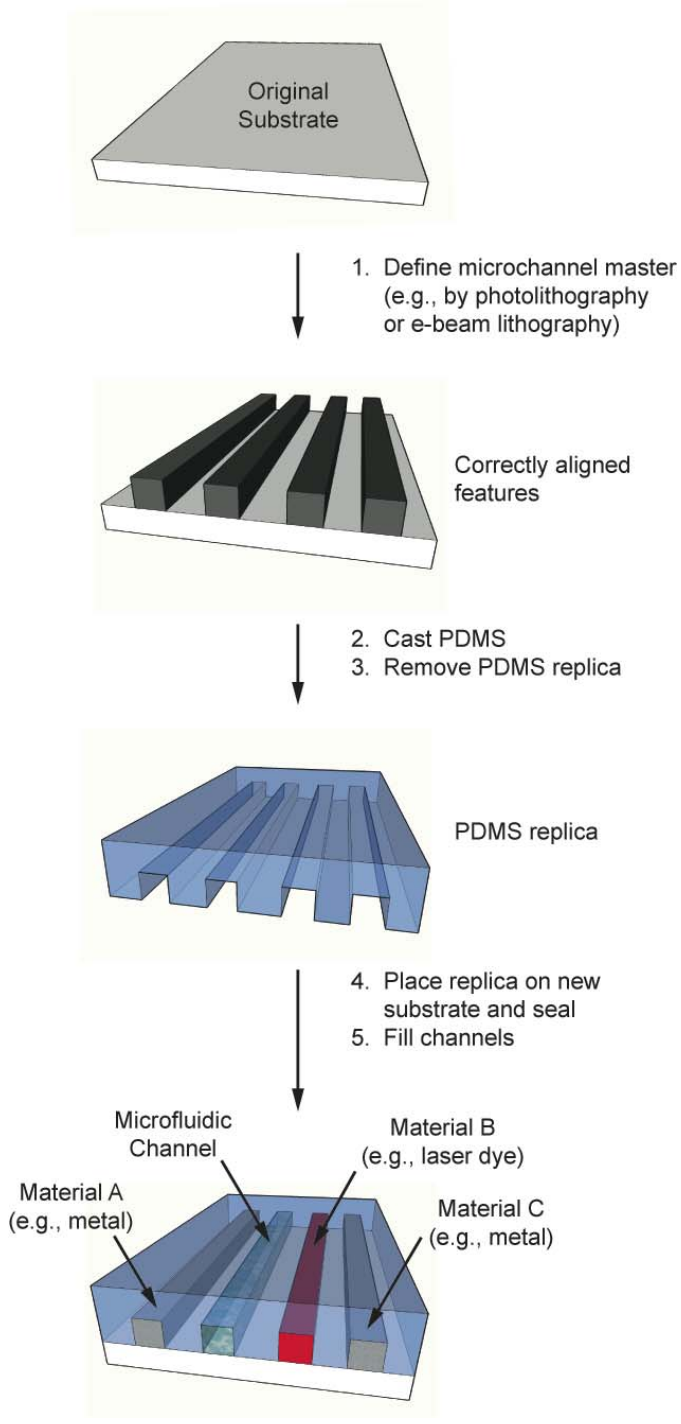

Original Substrate
1. Define microchannel master (e.g., by photolithography or e-beam lithography)
Correctly aligned features
2. Cast PDMS
3. Remove PDMS replica
PDMS replica
4. Place replica on new substrate and seal
5. Fill channels
Microfluidic Channel
Material B (e.g., laser dye)
Material A (e.g., metal)
Material C (e.g., metal)

Table 1. Properties of materials used to form microfluidic channels in co-fabricated systems.

Table 1

Material for Forming Channels	Method for Forming Channels	Advantages	Disadvantages
PDMS	SL	fast prototyping, biocompat. well studied, transparent, flexible/unbreakable	gas perm., melts at high temp, hydrophobic, absorbs small molec., swells with solvents
Polycarbonate	µM, IM, HE, e-B, LL	non-gas perm. struct. strong, transparent	hydrophobic, susceptible to organic acids/bases, inflexible
Polymethylmethacrylate	µM, IM, HE, e-B, LL	non-gas perm. struct. strong, transparent, cheap	hydrophobic, susceptible to organic acids/bases, inflexible
Cycloolefin Copolymer	µM, IM, HE, e-B	non-gas perm., cheap, resists solvents and acids/bases	hydrophobic
Perfluoropolyethers	µM, IM, HE	biocompat. resists solvents and acids/bases, liq. at R.T.	gas perm., not commercially available, requires UV to cure
Polyurethanes	SL	non-gas perm., easy to make hydrophilic, cheap flexible/unbreakable	more complex fab. than PDMS, difficult to bond layers or perform surface modifications
Silicon	µM, e-B, LL	well-studied, non gas-perm. resists solvents and most acids/bases	breaks easily, not electrically insulating, expensive, opaque
Glass	µM, e-B, LL	cheap, resists solvents and most acids/bases, non gas-perm., transparent	breaks easily, difficult to etch (req. HF) and seal to itself (req. high temp)
Thiolene	SL	fast prototyping,resists, cheap, solvents, transparent, low gas perm., biocompat.	requires UV to cure

SL = Soft Lithography, µM = Bulk/Surface Micromachining, IM = Injection Molding, HE = Hot Embossing, e-B = E-Beam Lithography, LL = Laser Lithography

Table 2. Relationship between the function of a co-fabricated microsystem and the material injected in its microfluidic channels.

Table 2

Function Class	Function	Phase	Material in Microfluidic Channel
Fluidic	Control and handling of liquid chemicals	Liquid	Aqueous-based solvents, buffers [21,22,30,31]
	Control and handling of biological samples for diagnostics	Liquid	Blood serum, saliva, other bodily fluids [12,32,33]
	Supply of nutrients to cell cultures	Liquid, Gel	Liquid-based media, Agar [25,26]
		Gas	Oxygen, CO_2 or other bio-active gases
	Supply of nutrients to multi-cell organisms	Liquid	Liquid-based media [27]
	Application of pressure for valves / pumps	Gas	Air or other inert gases
		Gel	pH responsive hydrogels [48]
	Colorimetric molecular sensing	Gel	Polydiacetylene-based hydrogel [49]
	Compartmentalization of reactions	Emulsion	Aqueous detergents suspended in fluorinated carrier fluids [63,64]
	Molecular crystallization	Emulsion	Aqueous detergents suspended in fluorinated carrier fluids [20,65]
Electronic	Conduction of electrical current (wires, circuits, antennas)	Solid	Low-melting-temperature metals [14]
	Generation of heat / control of temp.	Solid	Low-melting-temperature metals [14]
	Generation of electrostatic fields (dielectrophoresis, cell lysis)	Solid	Low-melting-temperature metals
	Generation of magnetic fields	Solid	Low-melting-temperature metals [36,37]
	Molecular electronics / testing of SAMs	Liquid	Non-Newtonian fluidic metals (EGaIn) [35,44,45]
	Electro-mechanical fluid actuation	Sol	Ferrofluids
Electrochemical	Storage of electrical energy (batteries)	Liquid	Electrolytes or conductive liquids
	Electroplating / electrochemical reactions	Liquid	Electrolytes or conductive liquids
	Electrophoretic separation	Gel	Polyacrylamide or agarose gels [46,47]
	Electrochromatographic separation	Sol-Gel	Porous photopolymerized sol-gel [15]
Optical	Guiding and switching light (waveguides)	Liquid	Liquids with high/low index of refraction [38,39]
	Focusing light (lenses)	Liquid	Liquids with high/low index of refraction [40]
	Generation of light (lasers, optical sources)	Liquid	Fluorescent or phosphorescent dyes [41,42]
	Diffraction of light (diffraction gratings)	Foam	Gas-liquid foams [62]
Structural	Micromechanical support (scaffolding)	Solid	Epoxies, cements, UV/heat curable polymers, or low melting-point metals [14,16-18]
	Solid support for bead packing and chromatography	Solid, Gel	Porous polymer and gel-based monoliths [16]
	Support for plant growth (hydrostats / artificial soils)	Gel	Sodium / potassium / ammonium polyacrylates
	Tissue engineering	Gel	Collagen, gels, other biocompat. solids [19,50-55]

Figure 2. Filling microchannels with low-melting temperature solders (microsolidics). (a) Schematic diagram describing the injection of low-melting point solders in microchannels. b) A metallic wire (100% In, width = 200 μm, height = 100 μm) embedded in a PDMS substrate; the wire can be twisted while still maintaining electrical conductivity (adapted from [14]). c) Mesh structures formed by injecting metal in PDMS microfluidic chambers. d-e) A system of three microfluidic channels, each filled with a different low-melting temperature material. In d), the outer channels are filled with 100% In metal, and the central channel is filled with a Bi56/Pb44 solder. In e), the outer channels are filled with 100% In metal, and the central channel is filled with 100% Se (a semiconducting non-metal); the three channels are connected together electrically, and form a metal-semiconductor-metal junction.

Figure 2

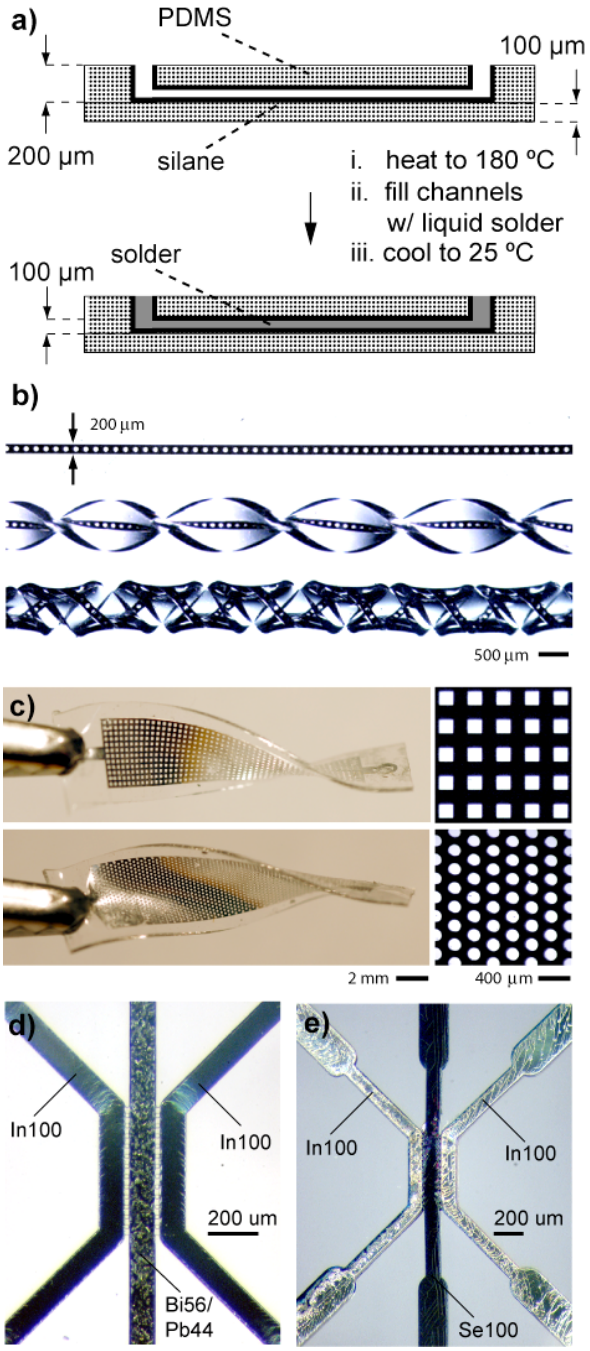

a)
PDMS
100 µm
200 µm
silane
i. heat to 180 ºC
ii. fill channels
w/ liquid solder
iii. cool to 25 ºC
solder
100 µm
b)
200 µm
500 µm
c)
2 mm
400 µm
d)
In100
In100
200 um
Bi56/
Pb44
e)
In100
In100
200 um
Se100

Figure 3. Co-fabricated electromagnets. a) Photographs of three microfluidic channels as viewed from above at low magnification (left), high magnification (upper right) and the cross-section of the three channels (lower right) (adapted from [36]). The two outer channels, which form the electromagnets, are filled with solder (length = 1.5 cm, width = 120 μm, height = 40 μm), and the central channel for fluids (length = 1.5 cm, width = 40 μm, height = 40 μm). b) Passing electrical current through the outer metal wires generates a magnetic field; this magnetic field can be used to move superparamagnetic beads suspended in solution in the central channel. c) The capture and release of superparamagnetic beads in a microfluidic channel in proximity to the two electromagnets (in black) located on either side of a microfluidic channel. The arrows represent the direction of electrical current passed through the electromagnet; the current generated a magnetic field oriented into the plane of the page with greatest magnitude at the edge of the microfluidic channel closest to the electromagnet. The process was repeated over 1000 times with similar results.

Figure 3

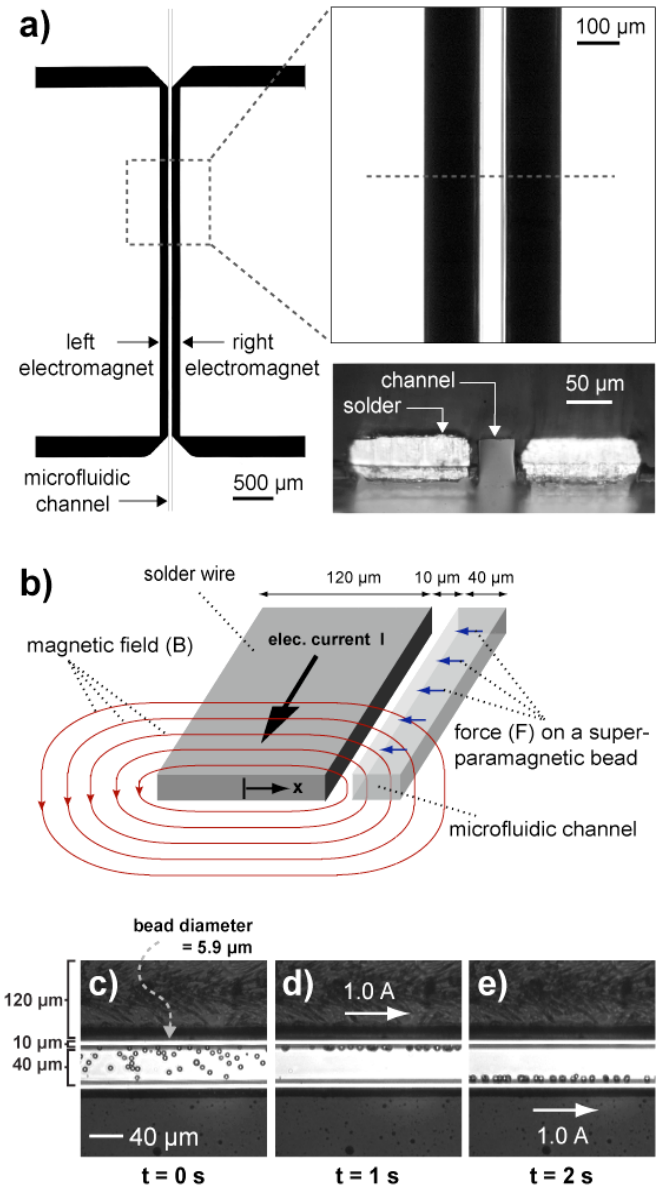

a)
100 µm
left
electromagnet
right
electromagnet
channel
solder
50 µm
microfluidic
channel
500 µm
b)
solder wire
120 µm
10 µm
40 µm
magnetic field (B)
elec. current I
force (F) on a super-
paramagnetic bead
x
microfluidic channel
bead diameter
= 5.9 µm
120 µm
10 µm
40 µm
c)
d)
1.0 A
e)
40 µm
1.0 A
t = 0 s
t = 1 s
t = 2 s

Figure 4. a) Schematic representation of the typical design of a L^2 waveguide. The index of refraction of liquid 2 is higher than that of liquids 1 and 3 for the guiding of light. Light is usually coupled into the liquid waveguide using optical fibers inserted into the PDMS device. b) Optical micrographs of the cross section of the outlet of the microfluidic channel viewed through the transparent window. The dashed box shows the location of the cross section of the microfluidic channel. The rates of flow (μL/min) (and the residence time in seconds) of the core and the cladding (clad) are listed. The guided light was from a fiber-coupled laser with l = 780 nm (adapted from [38]). c) Optical switch. (i)-(iii) Optical micrograph of the top view of the microfluidic channels. The dye in the core fluid makes allows it to be imaged; the dye is omitted in use. (iv)-(vi) Optical micrograph of the cross section of the end of the channel showing light exiting the L^2 waveguides. The white arrows and lines represent the location of the ends of the branches of the microfluidic channel.

Figure 4

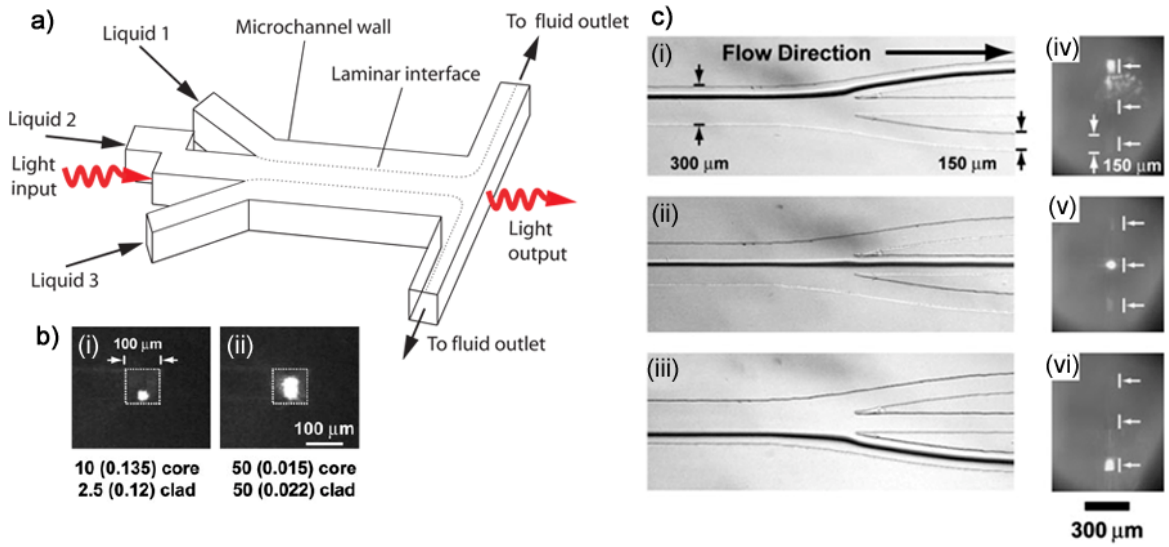

a)
Liquid 1
Microchannel wall
To fluid outlet
Laminar interface
Liquid 2
Light input
Light output
Liquid 3
To fluid outlet
b)
(i)
100 μm
(ii)
100 μm
10 (0.135) core
2.5 (0.12) clad
50 (0.015) core
50 (0.022) clad
c)
(i)
Flow Direction
300 μm
150 μm
(ii)
(iii)
(iv)
150 μm
(v)
(vi)
300 μm

Figure 5. a) Bright-field image an L^2 lens co-fabricated in a single layer of lithography. The laser beam from the fiber is visible in front of the aperture because PDMS contains nanoparticles of silica that scatter light. The focused beam in the beam-tracing chamber is visualized by the fluorescence of a rhodamine dye filling the chamber (adapted from [40]). b) Top-view scheme for the array of L^2 fluorescent light sources, consisting of parallel L^2 waveguides in a single PDMS microchannel. An end-coupled, tapered, liquid-core waveguide filled with DMSO collected the total fluorescence output. Inset: Optical micrograph of the T-junction. Dotted lines outline the walls of the PDMS channels. c) Spectral output (solid line) from an array of L^2 fluorescent light sources containing 0.5 mM solutions of perylene, fluorescein, and sulforhodamine B in DMSO/EG (1:1), with various cladding liquids: methanol ($n_{cladding} < n_{core}$); DMSO/EG (1:1, $n_{cladding} = n_{core}$); DMSO ($n_{cladding} > n_{core}$). Flow rates for all inputs were held constant at 4 mL/hr each (adapted from [41]).

Figure 5

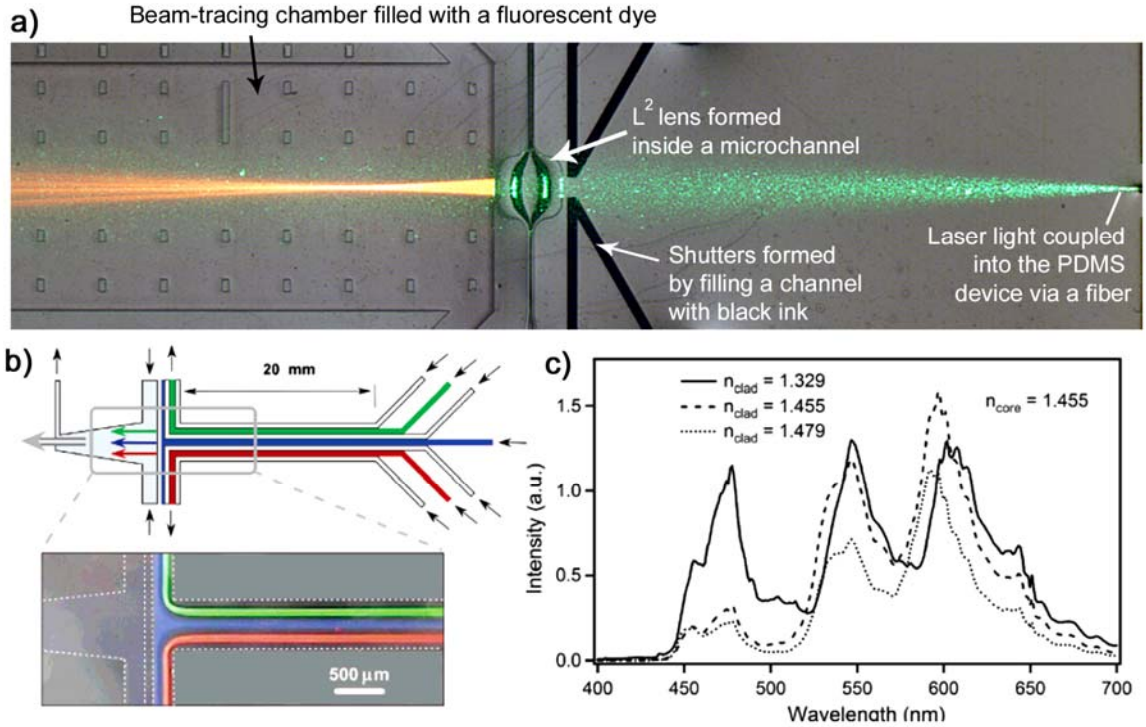

a)
Beam-tracing chamber filled with a fluorescent dye
L2 lens formed inside a microchannel
Shutters formed by filling a channel with black ink
Laser light coupled into the PDMS device via a fiber
b)
20 mm
500 µm
c)
n_clad = 1.329
n_clad = 1.455
n_clad = 1.479
n_core = 1.455
Intensity (a.u.)
0.0
0.5
1.0
1.5
400
450
500
550
600
650
700
Wavelength (nm)

Figure 6. Co-fabrication of molecular electronic devices in microfluidic channels. a) Schematic of the fabrication of the metal–SAM//EGaIn junctions. b) Top-down micrograph of two TS Ag-electrodes (of seven total) with EGaIn in the perpendicularly aligned PDMS channel. The PDMS is transparent and therefore cannot be seen in these images. c) The average values of the current density (*J*) as a function of voltage (V) applied across the junction. The shape of the J/V curve is asymmetric: the difference in average slope of *J* for negative values of V and positive values of V illustrates the rectification of electronic signals through the device (adapted from [44]).

Figure 6

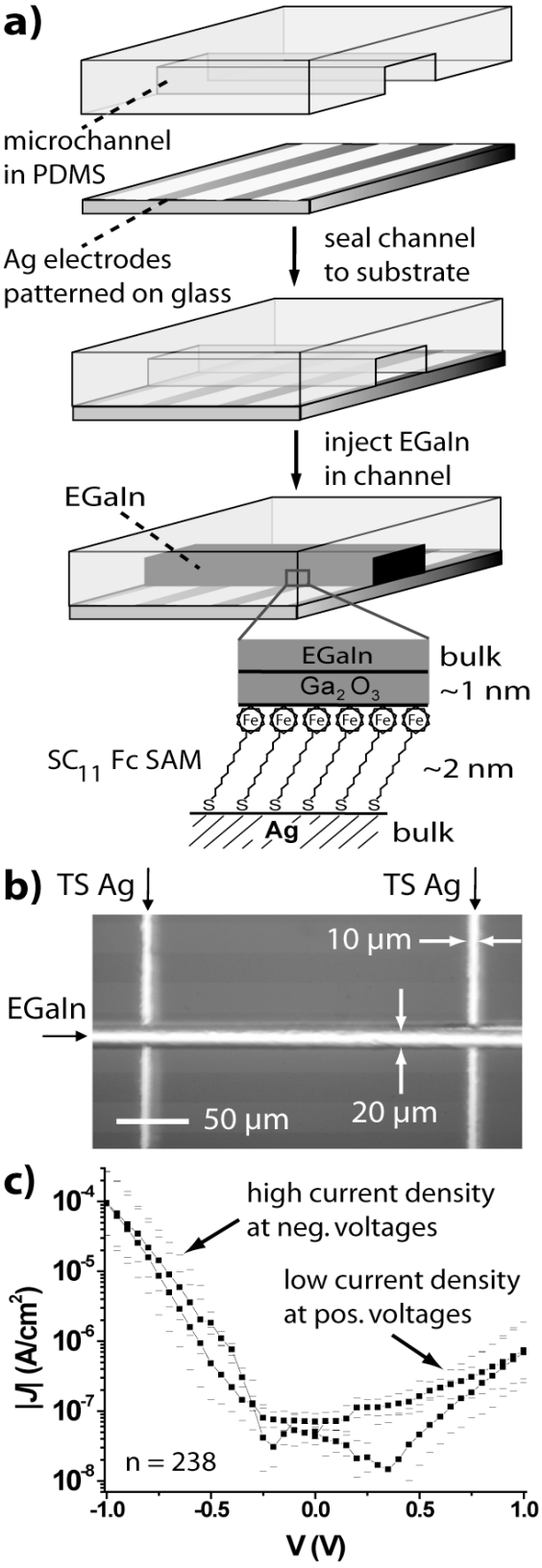
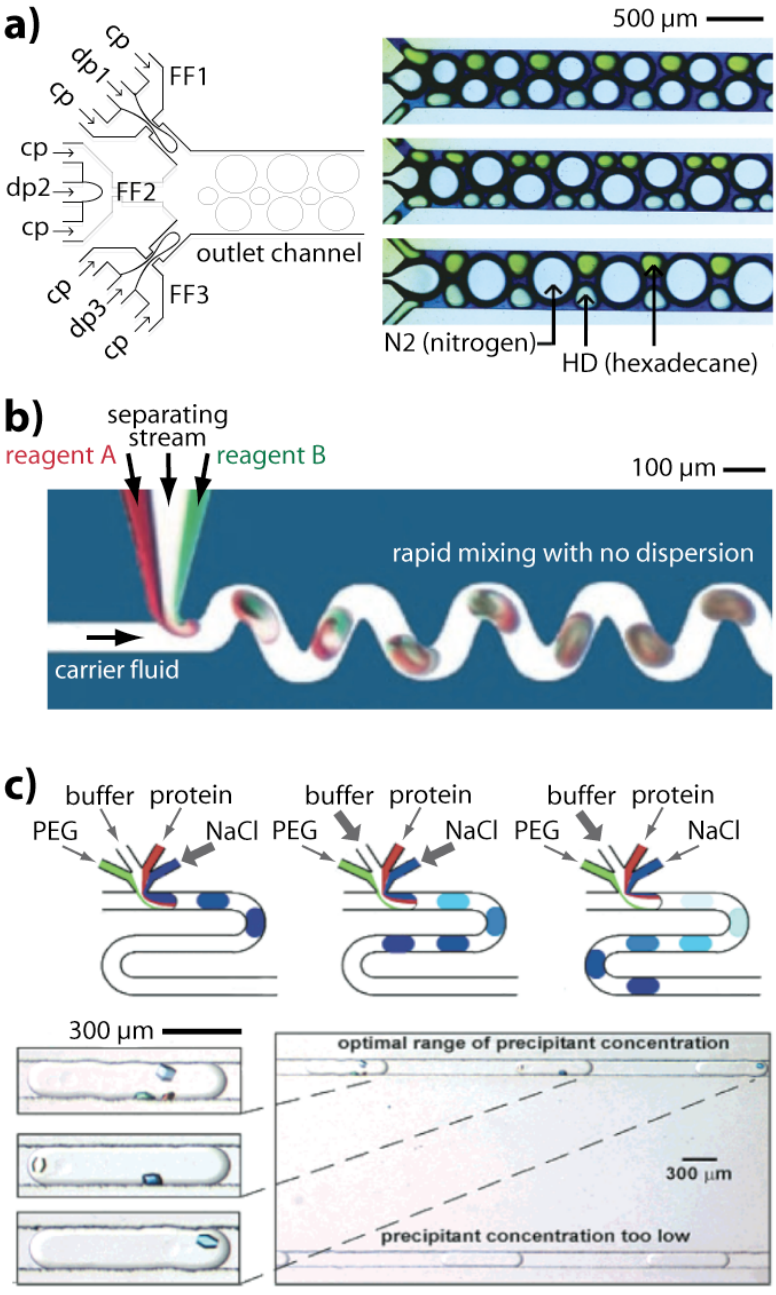

a)
microchannel
in PDMS
Ag electrodes
patterned on glass
seal channel
to substrate
inject EGaIn
in channel
EGaIn
EGaIn
bulk
Ga_2O_3
~1 nm
Fe
SC_{11} Fc SAM
~2 nm
Ag
bulk
b)
TS Ag
TS Ag
10 μm
EGaIn
50 μm
20 μm
c)
high current density
at neg. voltages
low current density
at pos. voltages
n = 238
|J| (A/cm²)
V (V)

Figure 7. Co-fabrication of emulsions in microfluidic channels. a) Complex lattice of emulsions. (left) A schematic representation of three flow-focusing generators connected to a single outlet channel. The abbreviations in the figures, cp and dp, denote the inlets of continuous phases and dispersed phases, respectively. The arrows indicate the direction of the flow of each phase. (right) Optical micrographs of composite lattices comprising nitrogen bubbles and hexadecane droplets suspended in water (adapted from [61]). b) Using droplets as microreactors. Aqueous droplets were formed containing two reagents and a separating stream containing buffer. The droplets were encapsulated in a fluorinated carrier fluid, which allowed them to be transported through the microchannels (adapted from [63]). c) Crystallization in droplets. (top) A schematic illustration for the droplet forming process: decreasing the flow rate of the NaCl stream and increasing the flow rate of the buffer stream increases the concentration of NaCl in each droplet. (bottom) A polarized microphotograph showing crystallization of lysozyme inside 7.5-nL aqueous droplets containing PEG, salt, lysozyme, and acetate buffer with variable composition (adapted from [65]).

Figure 7


a)
cp
dp1
cp
FF1
cp
dp2
cp
FF2
outlet channel
cp
dp3
cp
FF3
500 µm
N2 (nitrogen)
HD (hexadecane)
b)
separating stream
reagent A
reagent B
100 µm
rapid mixing with no dispersion
carrier fluid
c)
buffer protein
PEG
NaCl
buffer protein
PEG
NaCl
buffer protein
PEG
NaCl
300 µm
optimal range of precipitant concentration
300 µm
precipitant concentration too low